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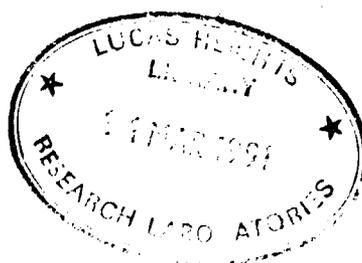
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REPORT

MRL-R-1148

THE DIRECT MEASUREMENT OF HETERONUCLEAR CHEMICAL
SHIFTS RELATIVE TO TETRAMETHYSILANE

A.G. Moritz



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ABSTRACT

The measurement of heteronuclear chemical shifts using absolute frequencies of the heteronucleus and the ^1H resonance of tetramethylsilane has been examined. This method avoids the problems associated with external standards and gives results which can be obtained quickly and with high precision. The method has a number of advantages in the accurate measurement of chemical shifts, as for example ^{31}P in chemical warfare agents and related chemicals and allows multinuclear data to be obtained without dynamic range or potential interference problems.

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1. INTRODUCTION

The implementation of a new chemical weapons treaty will require verification of non-production, non-stockpiling and use of known or potential chemical warfare agents. As part of any verification procedure, unambiguous identification of various organic chemicals, including chemical warfare agents and their precursors and breakdown products, will be required. This report examines methods of multinuclear NMR measurements, as for example ^1H , ^{13}C and ^{31}P , of such chemicals and forms part of the task "Technical Support for Chemical Disarmament" for the Department of Foreign Affairs and Trade.

The measurement of ^1H and ^{13}C chemical shifts in nonaqueous solvents is almost universally referenced to internal tetramethylsilane (TMS). ASTM Standard E386, has adopted TMS as the primary internal reference for these nuclei although no recommendations are made for other nuclei other than external references for boron (^{10}B and ^{11}B) and phosphorus (^{31}P) spectra [1]. In the latter case, the primary external reference is phosphorus oxide (P_4O_6) whereas almost all literature values are reported relative to external 85% phosphoric acid [2]. In general, external references are not satisfactory for several reasons namely: (1) lower precision than inert internal references, (2) dynamic range problems where both concentrated and trace detection is required and (3) difficulties in manipulation of toxic and or air sensitive materials where ^1H , ^{13}C and ^{31}P spectra are required from the one sample.

During the course of examination of some phosphorus compounds it was observed that large errors (~ 1 ppm) can arise for ^{31}P chemical shifts using external phosphoric acid. In these circumstances, positive identification of phosphorus containing compounds based solely on literature values could be unsatisfactory.

This report examines the direct measurement of heteronuclear chemical shifts using sequential measurement of the heteronucleus followed by measurement of the ^1H frequency of internal TMS. The derived values are equivalent to the δ values which were originally used to measure chemical shifts by heteronuclear spin-decoupling [3].

2. EXPERIMENTAL

All measurements were made on a Bruker AM 300 Spectrometer equipped with a 10 mm broad band probe. Resonance frequencies of the ^1H and X nuclei were derived directly from peak maxima using the existing DISR software. This information is available from the SF parameter and is limited to a precision of 0.1 Hz [4]. The acquisition parameters of sweep width and number of time domain points were adjusted in each case to allow a digital resolution of 0.03 Hz or better.

Sufficient leakage occurs between the transmitter and receiver circuits with the probe tuned to deuterium to allow the lock frequency to be derived directly with a dummy acquisition (pulse width equal to zero). For the AM 300 spectrometer, this occurs at 46.072 631 6 MHz, relative to the internal 10 MHz reference. This frequency was confirmed by measurement of chloroform-d in the unlocked mode with the field adjusted to be on resonance for the deuterium signal. The measurement of the deuterium lock frequency is only required where the δ values are derived from the lock reference using the method of Harris and Kimber [5].

Chemical shifts were measured in dilute solutions (< 1%) except where otherwise indicated. Samples were standard laboratory chemicals except for methyl methylphosphonfluoridate which was generated in-situ from a methylphosphonic dichloride, methylphosphonic difluoride mixture in CDCl_3 by addition of 0.2 μl of methanol. Phosphorus oxide was a commercial sample (Albright and Wilson) supplied in a 5 mm o.d. tube.

3. RESULTS

Measurements made on the ^{13}C and ^1H resonance frequencies of tetramethylsilane (TMS) in chloroform-d over a period of time (six months) with a variety of solutes indicated a long term reproducibility of better than ± 0.05 ppm. In part, these variations arise from the temperature sensitivity (Table 1) and cases where high solute concentrations are involved.

The reproducibility was not observed to be particularly sensitive to shimming conditions. This situation is to be expected as any asymmetry in line shape as a result of incorrect shimming will be observed for both the ^1H and X nuclei. The measurement of the peak maximum, which is necessarily a subjective assessment, is likely to be made in the same way. Similar considerations apply to adjustment of the necessary phase corrections after Fourier Transformation of the free induction decay.

The general problem of systematic errors in the chemical shift measurements is not easily resolved. A commonly used configuration in an X nucleus (multinuclear) probe is to employ one coil for the X nucleus and a separate double tuned coil for the ^1H and lock signal (normally ^2H). One type of systematic error which can arise is where the effective volume of the sample is different for the two coils and a field gradient exists. For a multinuclear probe where both the inner and outer coils can be tuned to a common nucleus (e.g. ^2H), this measurement is straightforward in either the locked or unlocked mode of operation. Measurements with our system with either acetone-d₆ or chloroform-d indicated that under normal shimming conditions, any difference was below the resolution of the combined hardware and software system (0.1 Hz, i.e. 0.002 ppm).

TABLE 1

 ^{13}C Chemical Shifts of Tetramethylsilane in Various Solvents

Temperature	Solvent		
	Acetone- d_6	Chloroform-d	Tetramethylsilane*
300	25.144 996 9	25.145 018 9	25.145 004 3
325	25.144 994 7	25.145 016 0	-

E

Scale corresponding to a resonance frequency of exactly 100 MHz for the ^1H nuclei of tetramethylsilane as internal standard.

* At 295 K.

In principle, the problem of systematic errors with separate measurement of the ^1H (of TMS) and X nucleus frequencies of the present method under locked conditions and that of any double resonance or multipulse experiment should be similar given that the same basic configuration of the hardware is involved. Possible exceptions to this situation arise where high power ^1H decoupling is used to obtain a single resonance for the X nucleus or a double tuned coil is used for both lock and pulsed observation. Measurements using broad-band, composite pulse and single frequency decoupling at various power levels as well as fully coupled spectra did not reveal systematic errors from this source. No systematic errors could be determined from the Fourier Transform process itself, i.e. the same results were obtained for the absolute ^1H frequencies with any combination of the basic spectrometer frequency (SF0) and "01", including the condition where SF0 is set "exactly" on frequency [4].

Attempts to compare the present method of measurement with previous double resonance experiments in real time is complicated by the absence of suitable data under well defined conditions. Table 2 shows a comparison of the sp^2 carbon in normal acetone relative to TMS for the present method and a pulsed INDOR measurement. The difference (0.36 - 0.74 ppm) is outside the combined experimental uncertainties even allowing for the unknown temperature conditions for the literature value. An examination of this problem indicated, however, that the chemical shift is quite sensitive to the amount of water present and therefore no firm conclusion can be drawn from this comparison.

For trimethyl phosphite, the results were indistinguishable from the early results of Baker and Burd [7]. A comparison with the INDOR results indicates a small difference which corresponds within experimental error to a shift in the proton frequency of $0.5 \text{ }^3\text{J}_{\text{PH}}$ (5.3 Hz) [8]. Presumably a similar offset occurs for the pulsed INDOR experiment with acetone where $^3\text{J}_{\text{CH}} = 5.92 \text{ Hz}$ [6].

TABLE 2

 ^{13}C and ^{31}P Chemical Shifts for Acetone and Trimethyl Phosphite (Neat Liquid^c)

Compound	Temperature	Ratio	
Acetone* (C = 0)	300	25.150 173 7	This work
	325	25.150 164 1	This work
	-	25.150 155 1	†
Trimethyl Phosphite ^{††}	300	40.486 280 9	This work
	-	40.486 280 9	++
	-	40.486 284 6	#

* Ratio is relative to ^1H of internal tetramethylsilane

† Reported by Freeman [6]

†† Ratio is relative to ^1H of trimethyl phosphite

++ Direct measurement, reported by Baker and Burd [7]

INDOR measurement, reported by Baker et al [8]

The results for the ^{13}C chemical shifts of TMS are shown in Table 1, from which it will be observed that there is a comparatively large chemical shift difference (0.87 ppm) between the solvents acetone- d_6 and chloroform- d . The value for tetramethylsilane, which is generally considered to be an "inert" solvent has an intermediate value. The values given in Table 1 may be compared with that of 25.144 995 MHz and 25.145 004 MHz reported by McFarlane [3] and Harris and Kimber [5] respectively. In both cases, the solvent, if any, or the temperature were not specified.

While the present results suggest that any X nucleus chemical shift can be referenced directly to internal TMS, several problems exist for measurement of ^{31}P chemical shifts. The first difficulty arises from the fact that virtually all compilations of chemical shift data are reported relative to external 85% phosphoric acid [2, 9], whereas the ASTM standard (E386) recommends phosphorus oxide (P_4O_6) [1]. Suitable conversion factors are therefore required to relate the present method with these standards and to those measurements of chemical warfare agents and related compounds reported relative to external $\text{P}(\text{OH})_4^+ \text{ClO}_4^-$ [10,11].

TABLE 3

 ^{31}P Chemical Shifts Measured with External Standards

Compound	Solvent	External Standard	Temperature	δ	
H_3PO_4	-	P_4O_6	300	-114.52	This work
			-	-112.5	Reference 12
$\text{P}(\text{OCH}_3)_3$	CDCl_3	P_4O_6	300	27.07	This work
	Nil	"	300	26.67	This work
	Nil	"	-	27.1	Reference 12
	Nil	H_3PO_4	300	141.83	This work
	CDCl_3	"	-	141.70	This work
	?	"	-	139.7	Reference 2
$\text{OP}(\text{OC}_2\text{H}_5)_3$	Nil	H_3PO_4	300	0.13	This work
	CDCl_3	"	"	-0.42	This work
	"	$\text{P}(\text{OH})_4^+\text{ClO}_4^-$	"	-0.85	This work
	"	H_3PO_4	-	-1.5	Reference 9
	?	"	-	-1.0	Reference 2
CH_3POF_2	CDCl_3	$\text{P}(\text{OH})_4^+\text{ClO}_4^-$	300	24.12	This work
	"	"	-	24.1	Reference 11
	"	H_3PO_4	-	25.0	Reference 9
CH_3POCl_2	"	$\text{P}(\text{OH})_4^+\text{ClO}_4^-$	300	43.58	This work
	"	"	-	43.4	Reference 11
	"	H_3PO_4	-	44.4	Reference 9
$\text{CH}_3\text{PO}(\text{OCH}_3)\text{F}$	"	$\text{P}(\text{OH})_4^+\text{ClO}_4^-$	300	31.21	This work
	"	"	-	30.89	Reference 10
	"	H_3PO_4	-	31.1	Reference 9

* H_3PO_4 refers to 85% H_3PO_4 ; values are not corrected for bulk magnetic susceptibility.

Table 3 summarises several measurements on ^{31}P chemical shifts for external 85% phosphoric acid and phosphorus oxide. Given that a tolerance of approximately ± 0.1 ppm is required to identify an unknown compound with a literature value, the agreement is unsatisfactory. In some cases, the differences amount to 2 ppm where 85% H_3PO_4 is used as an external reference. Measurements made using phosphoric acid supplied by a different manufacturer or after a twofold dilution did not vary by > 0.1 ppm.

The differences between the present measurements of CH_3POF_2 , CH_3POCl_2 and $\text{CH}_3\text{PO}(\text{OCH}_3)\text{F}$ and those previously reported using $\text{P}(\text{OH})_4^+\text{ClO}_4^-$ as a reference do not exceed 0.3 ppm. It will also be observed from Table 3, that the previously reported chemical shifts using 85% H_3PO_4 [9] and $\text{P}(\text{OH})_4^+\text{ClO}_4^-$ [10, 11] as external standards vary over the range 0.2 - 1.0 ppm. Table 4 lists the observed ^{31}P chemical shifts of three external standards which are required if comparison is to be made with previously reported data or measurements made using the ASTM (E386) standard.

TABLE 4

Chemical Shifts* (δ) of ^{31}P Measured with External Standards relative to Internal TMS in CDCl_3 at 300 K

Compound	δ
H_3PO_4 (85%)	40.480 720 0
P_4O_6	40.485 359 0
$\text{P}(\text{OH})_4^+\text{ClO}_4^-$	40.480 737 3

* Not corrected for bulk magnetic susceptibility. The value for H_3PO_4 is not regarded as reliable (see text).

4. DISCUSSION

The present results indicate that under certain conditions, the use of the external standard, 85% phosphoric acid may lead to substantial discrepancies in the chemical shifts compared with those reported in the literature. In view of the fact that ^{31}P chemical shifts have been reported using this standard for approximately thirty years, it is surprising that the problems observed in the present investigation have not been reported previously. Crutchfield, Dungan and Van Wazer [13] found that for relatively low concentrations (~ 10 wt%) up to ~ 93%, beyond which point there are measurable amounts of pyrophosphoric acid in equilibrium with the orthophosphoric acid,

the relative chemical shift of H_3PO_4 remains constant within 0.1 ppm. It is unlikely, therefore, that the anomalies observed in the present investigation arise from the precise concentration of the phosphoric acid used. On the other hand, our measurements are in more reasonable agreement with the values reported for potential organophosphorus warfare agents using $\text{P}(\text{OH})_4^+\text{ClO}_4^-$ as an external standard. The use of $\text{P}(\text{OH})_4^+\text{ClO}_4^-$ as a secondary shift reference standard in ^{31}P NMR was originally proposed [14] because of its extremely narrow line width (~ 0.1 Hz). Glonek and Van Wazer [14] reported that the ^{31}P resonance in $\text{P}(\text{OH})_4^+\text{ClO}_4^-$ occurs 0.067 ppm upfield from the resonance of 85% H_3PO_4 . This value may be compared with that of 0.43 ppm downfield for the present work of 0.2 - 1 ppm downfield based on previously reported chemical shifts [9, 10, 11].

Current multinuclear NMR spectrometers normally adopt a synthesiser to generate all required observing frequencies. The internal reference standard used in the synthesiser is also used to generate other required frequencies such as the proton decoupling, local oscillator difference and lock reference frequencies which are phase coherent with the main synthesiser. In these circumstances, long term stability under locked conditions is guaranteed. As all X nuclei probes incorporate ^1H decoupling coils, direct measurement of any heteronucleus chemical shift in nonaqueous solutions relative to an internal standard (^1H of TMS) is possible. This method meets all the criteria for a "good reference" as recently discussed by Granger [15] and does not require lock correction and consideration of the effect of solute on locking as would be required by other methods which use the ϵ scale. In addition to the advantages of rapid measurement and high precision which is obtainable, the direct frequency measurement method, in common with other methods which use the ϵ scale, avoids the problem of a convention regarding the sign of the chemical shift difference.

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ABSTRACT

The measurement of heteronuclear chemical shifts using absolute frequencies of the heteronucleus and the ^1H resonance of tetramethylsilane has been examined. This method avoids the problems associated with external standards and gives results which can be obtained quickly and with high precision. The method has a number of advantages in the accurate measurement of chemical shifts, as for example ^{31}P in chemical warfare agents and related chemicals and allows multinuclear data to be obtained without dynamic range or potential interference problems.